

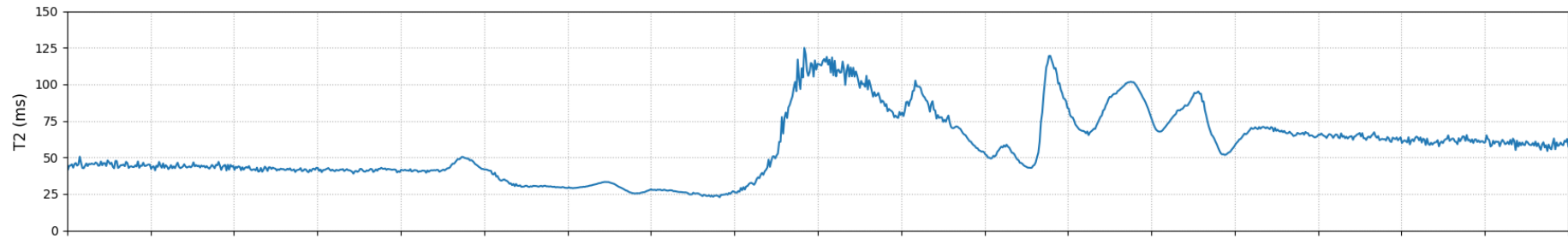
# Pointwise T2 fitting for spectral relaxography: examples in dystrophic and healthy muscle

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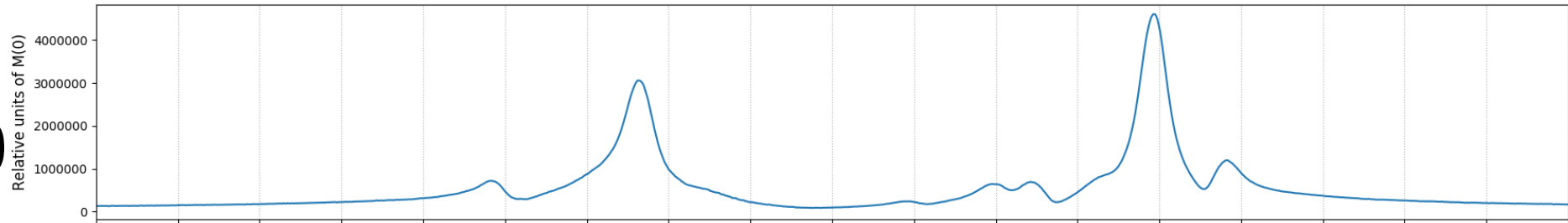
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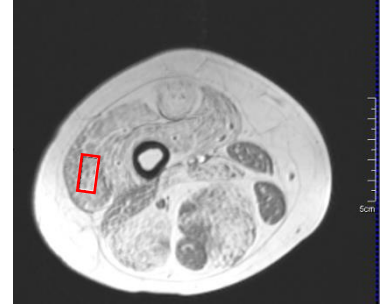
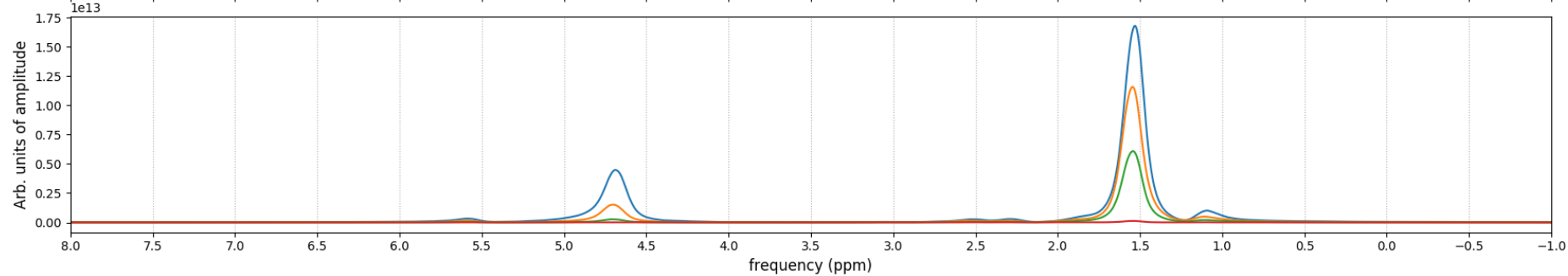
$T_2$



$M_0$



Stacked  
multi-TE  
spectra



SVS voxel in vastus lateralis of male with Duchenne Muscular Dystrophy (DMD)

Magnitude spectra at TE= 11ms, 27, 54, 243

## Introduction

Relaxation time constants can yield important biological information. Generating spatial parametric maps of  $T_1$  and  $T_2$  are well known MRI techniques. These maps usually involve fitting an exponential function to data points in the decay dimension for each image voxel. Chemical shift information is generally lost.

In NMR spectroscopy, MRS and MRSI, it is known that various spectral peaks often have different relaxation times. Previous single-voxel-spectroscopy (SVS) studies of muscle in DMD have shown that the  $T_2$  of the water signal changes in response to steroid treatment, and that the overall  $T_2$  of the muscle changes with disease progression.

Efforts to characterize the relaxation properties of magnetic resonance (MR) signals in the frequency domain have traditionally used either of two approaches:

- i) **parametric line-shape modeling**
- ii) **spectral integration over the range of a peak of interest**

These approaches involve possibly erroneous assumptions and may obscure useful information contained in the decay-dimension of a dataset.

Here, we demonstrate fitting every point in the frequency domain for a transverse relaxation time constant ( $T_2$ ) and equilibrium magnetization ( $M_0$ ), from which we generate plots of  $T_2$  and  $M_0$  as a function of chemical shift.

## Methods

While pointwise relaxation fitting in the frequency domain is potentially broadly applicable, the present results are from data of limited scope.

### Acquisition:

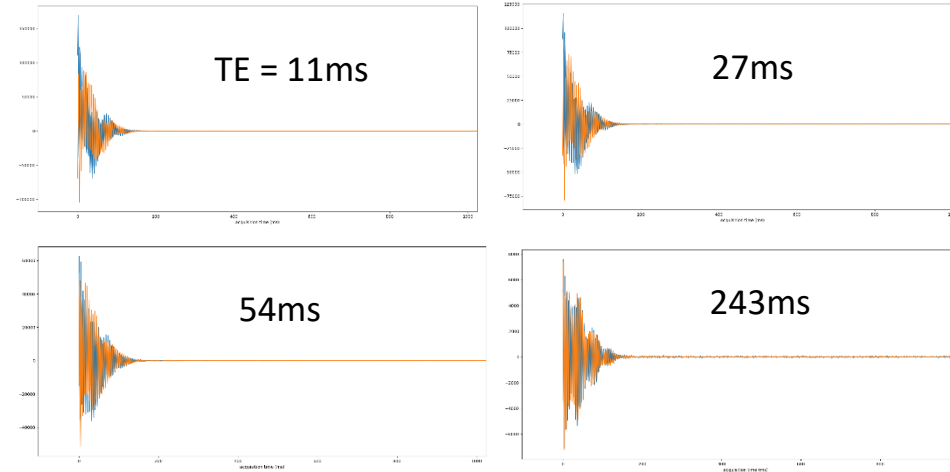
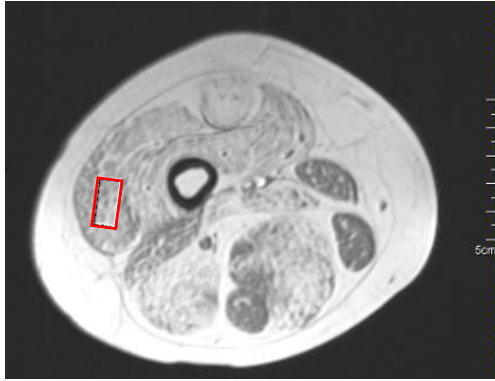
In vivo muscle data and phantom data acquired on a Siemens 3T whole-body MRI instrument with a STEAM SVS sequence.

For vastus lateralis data, TE = (11ms, 27, 54, 243).  
TR = 9000ms. Half-echo FID sampling of 2048 points for 1024ms. Water placed on-resonance.

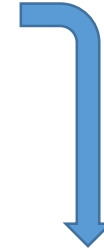
### Processing:

Custom python code incorporating apodization, peak alignment, automatic or manual phasing, zero-filling, and eventually pointwise relaxation fitting and plotting. Using existing libraries such as Numpy, Scipy, Matplotlib, pydicom, and NMR Glue.

STEAM single-voxel  
spectroscopy  
acquired in  
dystrophic vastus  
lateralis (VL) muscle



Time domain



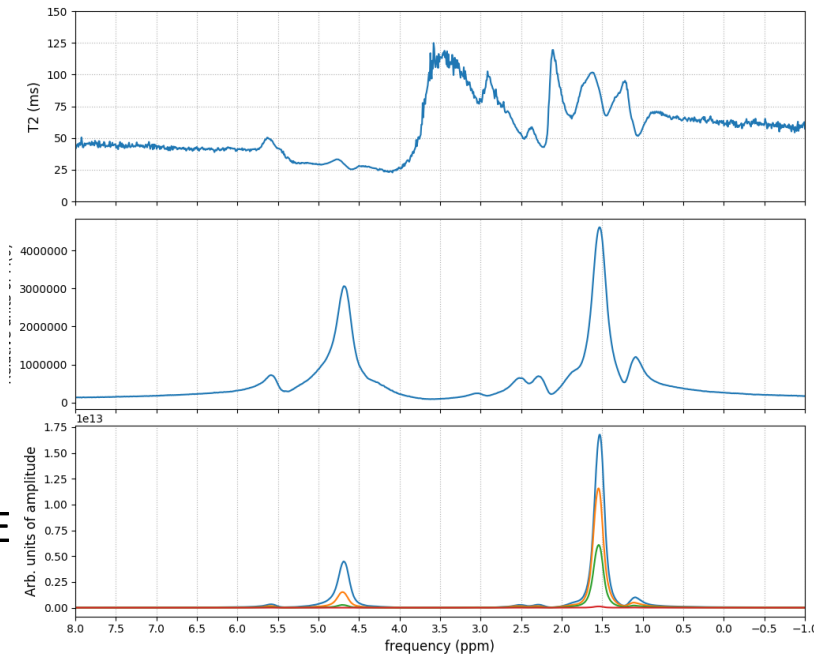
FFT

Take magnitude of  
complex spectrum  
(optional)

$T_2$

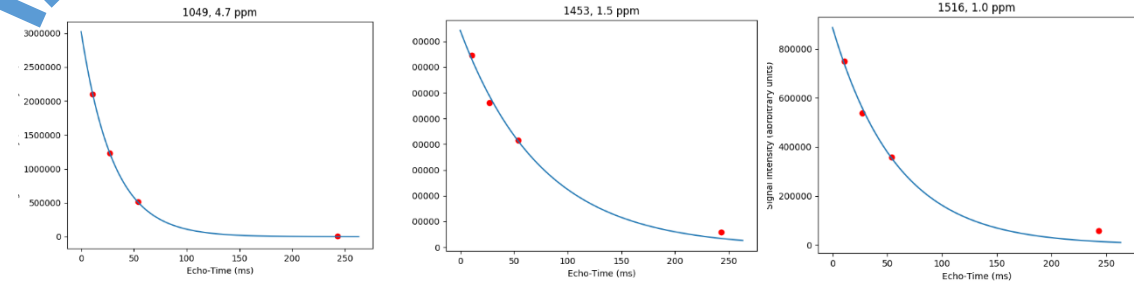
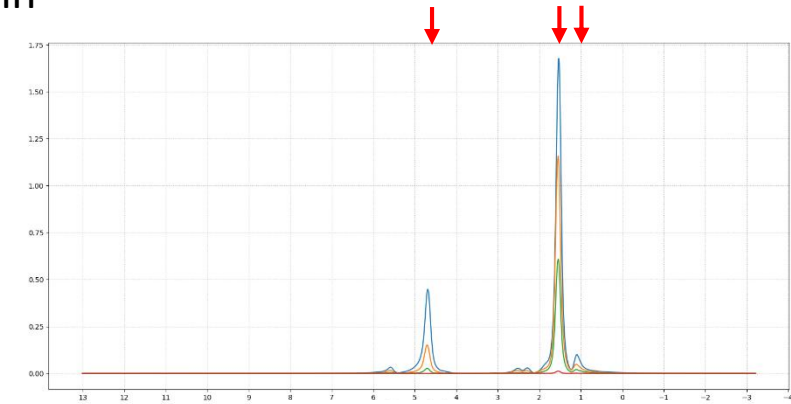
$M_0$

Stacked  
multi-TE  
spectra



Every point in the frequency  
domain fit for  $T_2$  and  $M_0$  and  
used produce plots of  $T_2$  and  
 $M_0$  as a function of frequency

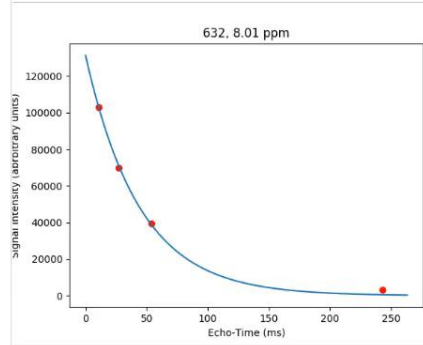
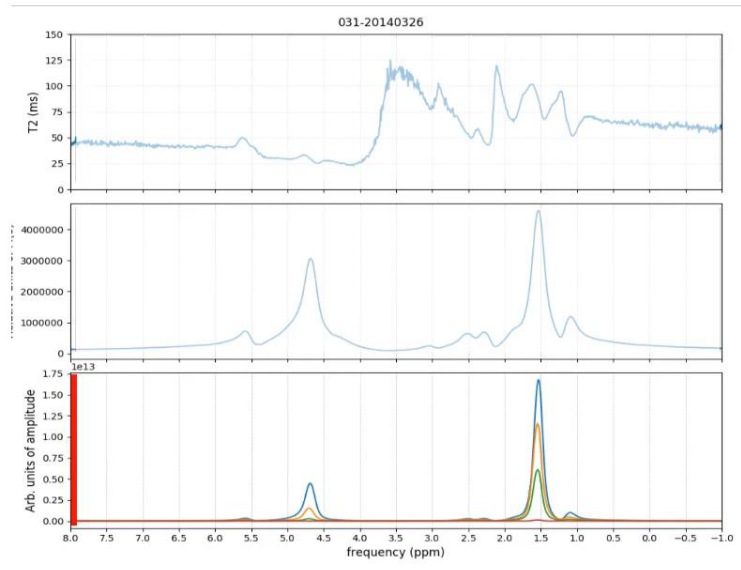
$$S(TE) = M_0 \cdot e^{-\left(\frac{TE}{T_2}\right)}$$



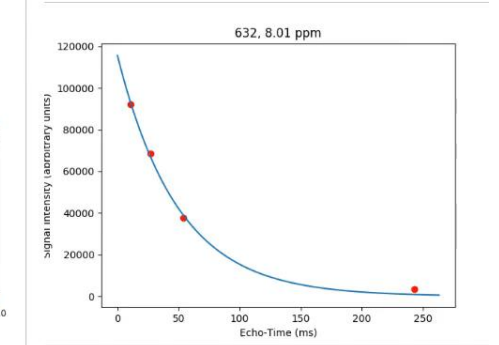
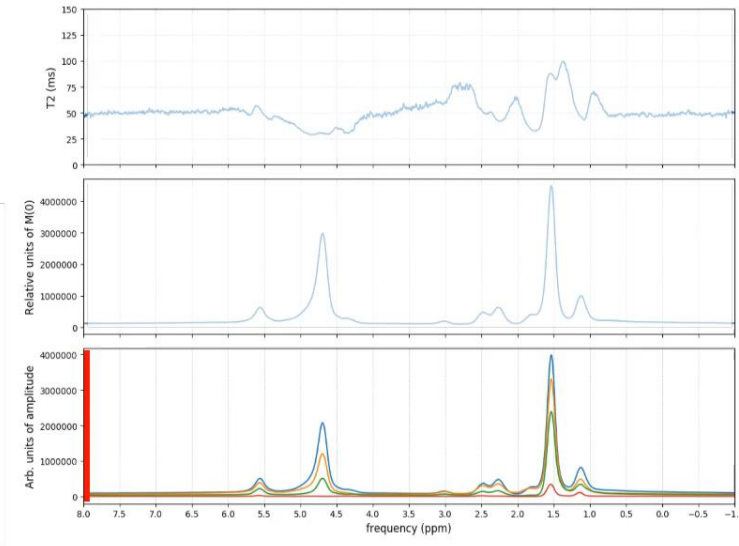
Decay dimension (Echo time)

...

## Magnitude



## Real

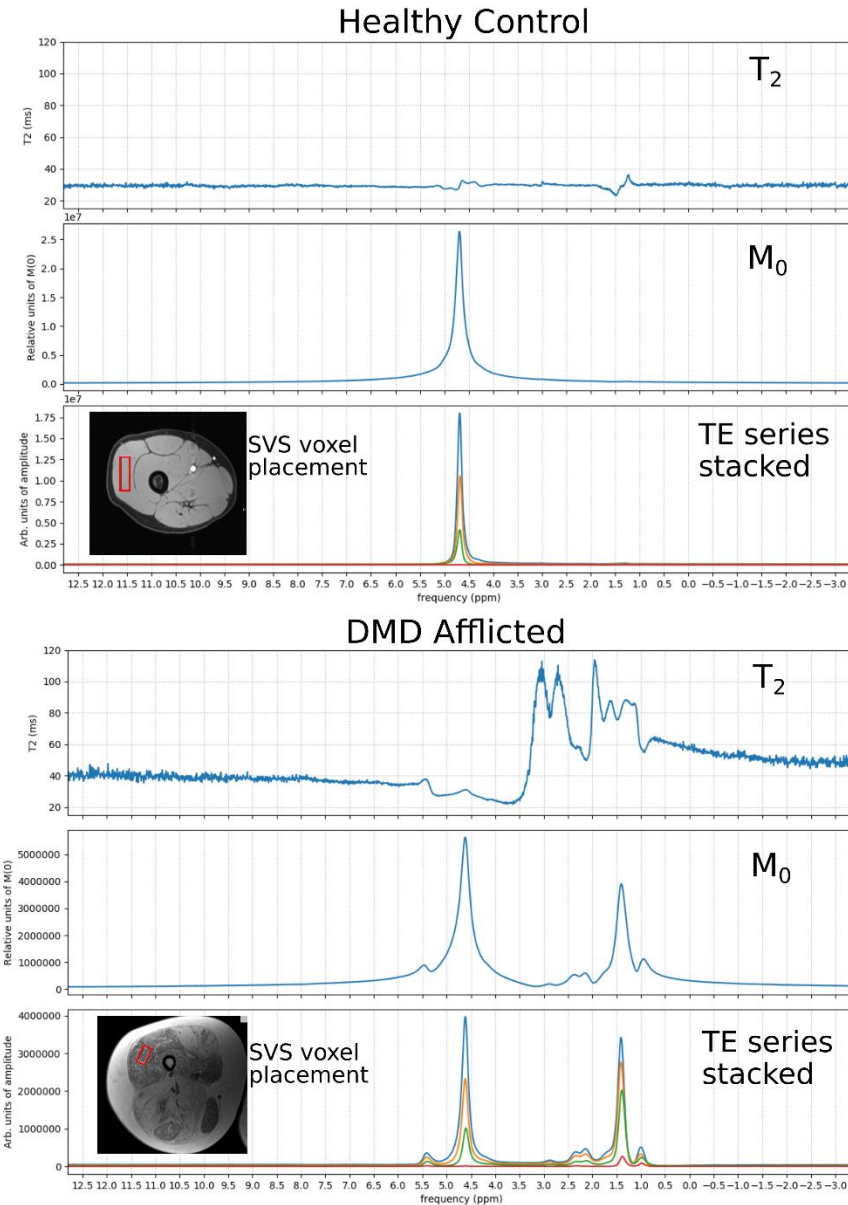


1 Hz exponential apodization on both magnitude and real

Taking the magnitude of the complex-valued spectral data following FFT has some advantages:

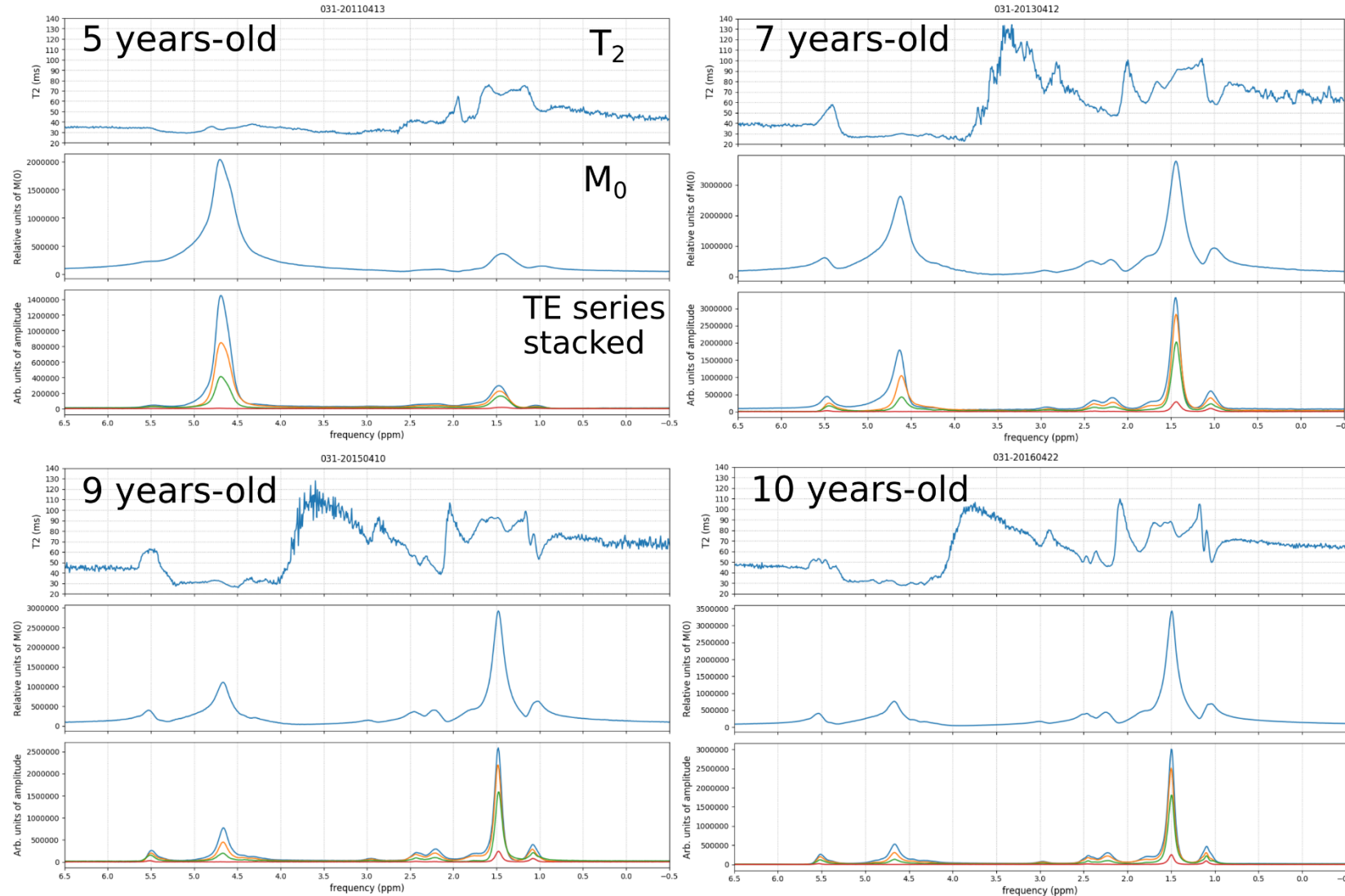
- 1) Phasing the spectrum to obtain a true “pure absorption mode” can be problematic, magnitude mode avoids this.
- 2) The baseline can exhibit artifacts that cause relaxation fitting to fail or become unstable, magnitude mode mitigates this.
- 3) In general, we have found highly stable results with magnitude mode fitting.

However, magnitude mode may introduce spurious relaxation time fittings between peaks that arise from interference in the dispersive channel.



Spectral T<sub>2</sub> comparison between VL in a 14 year-old healthy male (top) and an 11 year-old male with DMD (bottom).

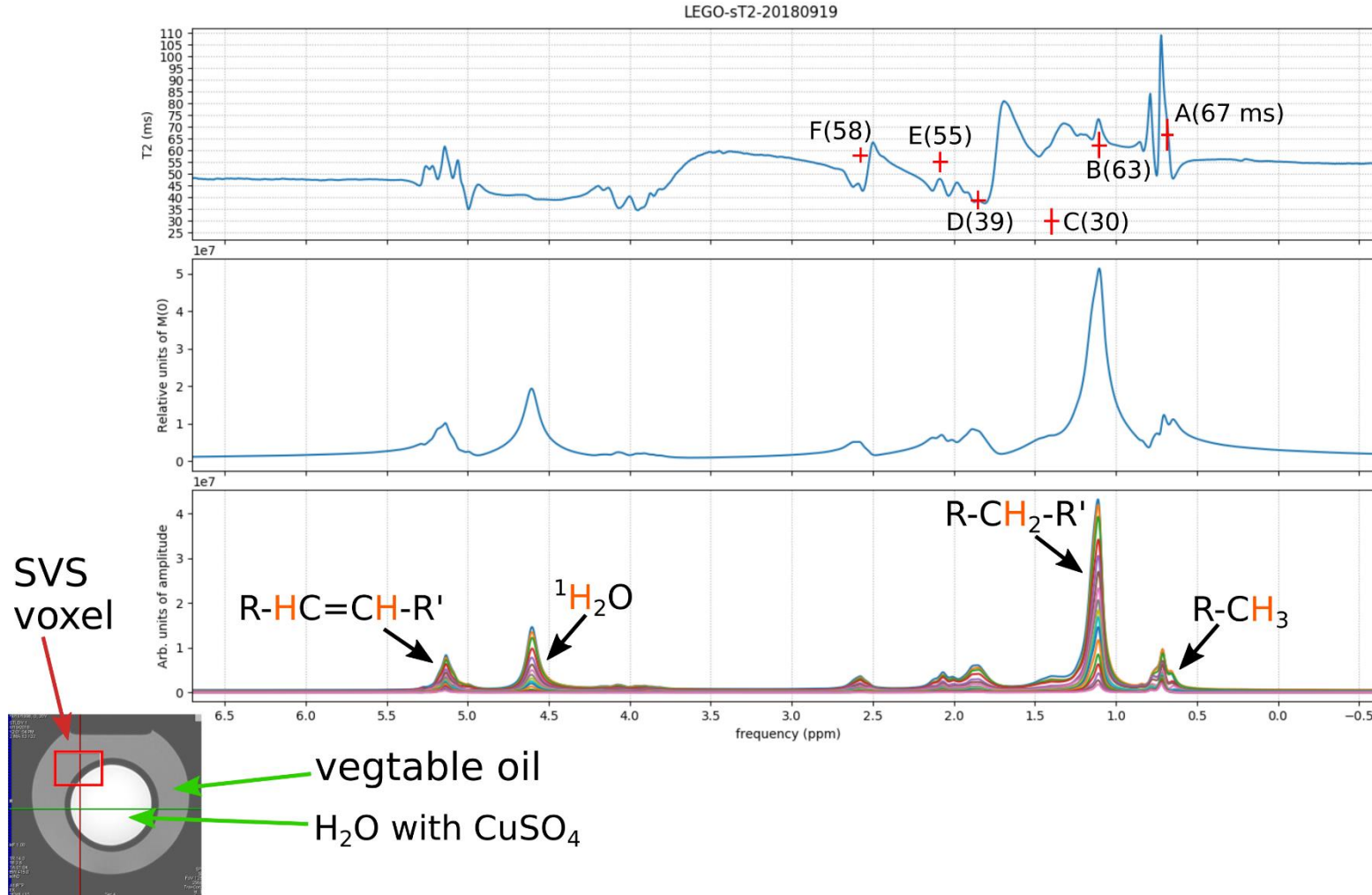
The water T<sub>2</sub> at the center of the spectrum is quite similar between these subjects at approximately 33ms, however the fatty-tissue replacement in the DMD subject reveals dramatic T<sub>2</sub> features at 2.7 and 3.5ppm as well as T<sub>2</sub> variability among the lipid resonances between 0.7 and 2.5ppm.



VL spectral T<sub>2</sub> plots for a male with DMD, longitudinally tracking rapid disease progression.

Only minor changes in the spectral T<sub>2</sub> are observed between 9 and 10 years-of-age. The prominent feature at approximately 3.5ppm is very clear and persistent in this subject.





Spectral T<sub>2</sub> plot from a vegetable oil phantom with 16 TE values (11 – 288 ms).

The cross marker overlays depict the T<sub>2</sub> values from subcutaneous adipose tissue at 7T as previously reported by Ren, et. al.<sup>2</sup>, and show remarkably close agreement for all lipid resonances with the exception of “C”. The inset at lower left shows the voxel placement in the cylindrical oil and water (LEGO) phantom.

## Results

Spectral pointwise  $T_2$  fitting was robust and reproducible, including at the tails of the spectral window where there is little obvious signal. The  $T_2$  of the dominant spectral component, often  $^1\text{H}_2\text{O}$ , determined the mean  $T_2$  values at the edges of the spectrum and indicate the broad extent of signal contribution. Variance of the  $T_2$  fit increases with spectral offset from the signal maximas.

VL  $^1\text{H}_2\text{O}$  (4.7ppm)  $T_2$  values were found to occur in the narrow range of 26 - 39ms, with DMD afflicted muscle showing a greater range that tended to decrease with disease progression (Figure 3). The lipid methyl resonance at 0.9 ppm had a  $T_2$  range of 55 - 90ms, and generally lower  $T_2$  than the methylene signals at 1.4 and 1.7 ppm. Creatine and trimethylamines are not well resolved but may contribute to the spectral  $T_2$  peaks at 3.0ppm and 3.2ppm. In the higher fat-fraction VL spectra, a large and broad  $T_2$  feature appears at 3.5ppm to 4.0ppm and warrants future investigation. Analysis of the oil and water phantom spectra shows highly similar  $T_2$  values for 6 lipid resonances previously studied (Figure 4).<sup>2</sup>

## Discussion

The ability to visualize a  $T_2$  spectrum aids in interpretation of complex signal behavior, and identification of overlapping signals. One motivation for pointwise  $T_2$  fitting was to better understand the spectral heterogeneity of  $^1\text{H}_2\text{O}$   $T_2$  in DMD, especially later in the disease when lipid is the dominant signal. At high lipid fractions, the apparent water  $T_2$  in muscle often decreases, and the contribution from the proximal lipid resonances does not appear to be the cause. The spectral  $T_2$  provides a unique fingerprint that conveys additional information on muscle pathology.

Future directions include a rigorous assessment of the relative benefits of fitting on real or magnitude spectra. The TE sampling scheme will be investigated as it may play a role in some of the spectral  $T_2$  features. Additionally, inversion recovery SVS acquisition can be used to generate a spectral  $T_1$ . A bi-exponential decay model may yield additional information and help to distinguish otherwise hidden spin populations. More work is required to link specific  $T_2$  features to normal and pathological biology.

These derived spectral relaxation plots may lead to unprecedented richness in relaxation analysis. This approach can readily be applied to other tissues in vivo, NMR spectroscopy in vitro, and coherent spectroscopy in general.



## Acknowledgements

This work was funded in part by:  
NIH NIAMS/NINDS R01AR056973  
NIH OD S10OD018224-01  
NIH OD S10OD021701

We would like to thank Manoj Sammi, Rob Mueller, and Thomas Barbara for helpful discussions.

## References

- [1] Mosconi, E. , Sima, D. M., Osorio Garcia, M. I., Fontanella, M. , Fiorini, S. , Van Huffel, S. and Marzola, P. (2014), Different quantification algorithms may lead to different results: a comparison using proton MRS lipid signals. *NMR Biomed.*, 27: 431-443. doi:[10.1002/nbm.3079](https://doi.org/10.1002/nbm.3079)
- [2] Ren, Dimitrov, Sherry, and Mallow. Composition of adipose tissue and marrow fat in humans by <sup>1</sup>H NMR at 7 Tesla, *Journal of Lipid Research*, 2008. 49: 2055-2062
- [3] Forbes, Sean C., et al. "Magnetic resonance imaging and spectroscopy assessment of lower extremity skeletal muscles in boys with Duchenne muscular dystrophy: a multicenter cross sectional study." *PloS one* 9.9 (2014): e106435.
- [4] Arpan, I., Willcocks, R. J., Forbes, S. C., Finkel, R. S., Lott, D. J., Rooney, W. D., ... & Finanger, E. L. (2014). Examination of effects of corticosteroids on skeletal muscles of boys with DMD using MRI and MRS. *Neurology*, 83(11), 974-980.
- [5] Rooney, William, et al. "Soleus muscle water T2 values in Duchenne muscular dystrophy: associations with age and corticosteroid treatment." *Proceedings of the 21st ISMRM Scientific Meeting, Salt Lake City, UT, USA*. Vol. 689. 2013.